

## REMARKS

In response to the Restriction Requirement mailed February 23, 2005, applicants elect Invention I, claims 1-9, drawn to methods of predicting the association of a test agent with zone 3 necrosis by expression profiling, without traverse.

Further, applicants provisionally elect the nucleic acid sequence of SEQ ID NO: 71 (TOXMARKER 71; cszr\_204152648\_191521095), with traverse. Applicants respectfully assert that the requirement to elect one single sequence for examination is improper for the reasons outlined below.

In essence, the invention requires that the expression of a sufficient number (but definitely more than one) of genes be determined in order to arrive at a statistically significant prediction of toxicity of a test agent. One skilled in the art would immediately appreciate that measurement of the expression of a single sequence in an attempt to predict zone 3 hepatic toxicity of a test agent would not provide a statistically significant prediction, and would thus render the claimed invention inoperable. Measurement of the expression of a number of sequences, which, *in combination*, provide a statistically significant prediction of toxicity, is therefore a necessary feature of the claimed invention (See page 5, lines 3-6 of the specification). For example, the specification teaches in Example 10 on page 149, that the smallest set of markers capable of predicting toxicity with acceptable statistical significance is a set of seven markers consisting of TOXMARKERs 42, 59, 65, 66, 71, 76 and 97.

Thus, applicants request that the sequence election requirement be withdrawn. Applicants submit the following suggestion for sequence election and examination. Applicants believe that TOXMARKER 71 represents a novel sequence. Thus, if TOXMARKER 71 is indeed found to be novel by the Examiner, any method claim which requires use of TOXMARKER 71 will necessarily be novel. In such case, the Examiner will only need to examine a single sequence (TOXMARKER 71), which does not represent an undue search burden. Accordingly, new claims 12-14 have been added which require the use of

Applicants: McCabe, et al  
U.S.S.N.: 10/663,418

TOXMARKER 71 in addition to at least one TOXMARKER selected from the group consisting of TOXMARKERS 1-70 and 72-132.

Applicants reserve the right to petition the sequence election requirement imposed by the Examiner.

Claims 10 and 11 have been canceled herein without prejudice as drawn to non-elected subject matter. Applicants reserve the right to pursue these claims in a later application. Claims 12-14 have been added. No new matter has been added. Upon entry of this amendment, claims 1-9 and 12-14 will be pending

Applicants: McCabe, et al  
U.S.N.: 10/663,418

## CONCLUSION

On the basis of the foregoing remarks, Applicants respectfully submit that this paper is fully responsive and that the pending claims are in condition for allowance. Such action is respectfully requested. If there are any questions regarding this response, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted on this 23rd Day of March, 2005



Daniel K. Rieger

Registration No. 56,436

CuraGen Corporation  
555 Long Wharf Drive  
New Haven, CT 06511  
Telephone: (203) 974-6271  
Facsimile (203) 401-3351